

Effects of sustained isometric handgrip on praecordial accelerocardiogram in normal subjects and in patients with heart disease

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The effects of isometric exercise on the maximum amplitude of the praecordial accelerocardiogram (as represented by the DE deflection) have been compared in 6 normal subjects (group 1), 12 patients with aortic stenosis (group 2), and 16 patients with myocardial disease (group 3). Whereas the tachycardia and pressor effects of isometric exercise were identical in all three groups, the normal subjects showed a significant decrease in DE during handgrip of 10 ± 4 per cent ($P < 0.05$) as compared with the insignificant increases of 8.5 ± 6 per cent ($P > 0.5$), and 4 ± 3.5 per cent ($P > 0.3$) observed in the patients in groups 2 and 3. This response in the normal subjects differed significantly from the responses observed in the patients in groups 2 ($P < 0.02$) and 3 ($P < 0.01$).

Of the patients in each of groups 2 and 3, 50 per cent responded abnormally to handgrip in that they showed a significant increase in DE. In the patients with aortic stenosis this subgroup of patients differed from the remainder in that they had a higher resting cardiac index ($P < 0.05$). In the patients with myocardial disease this subgroup was characterized by a significantly lower resting left ventricular end-diastolic pressure ($P < 0.02$). It seems, therefore, that those patients who increase DE in response to handgrip tend to have better left ventricular function at rest than those who do not. We suggest that this may be because of increased beta adrenergic activity at rest and during isometric exercise in the subgroup who respond to handgrip with an increase in DE.

Animal work has shown that peak acceleration of blood flow in the ascending aorta is highly sensitive to small changes in left ventricular contractility which are insufficient to cause changes in stroke volume or systemic blood pressure (Chung, Chamberlain, and Seed, 1974; Noble, Trenchard, and Guz, 1966a; Reuben and Littler, 1973; Winter *et al.*, 1967). It has also been shown in the dog that changes in the maximum amplitude of the praecordial accelerocardiogram correlate closely with changes in peak aortic acceleration in response to a wide range of manoeuvres (Reuben and Littler, 1973). Furthermore, it appears that both are relatively independent of heart rate and ventricular loading, at least in the intact organism (Noble *et al.*, 1972; Noble, Trenchard, and Guz, 1966a, b; Reuben and Littler, 1973).

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Isometric exercise, in the form of sustained handgrip, has been widely used as a stress test in cardiac laboratories for the detection of impaired left ventricular function (Helfant, De Villa, and Meister, 1971; Kivowitz *et al.*, 1971; Krayenbuehl *et al.*, 1972, 1973). Using the non-invasive technique of praecordial accelerocardiography we have previously demonstrated, in normal subjects, that the response to isometric exercise is independent of beta adrenergic mechanisms (Hume, Irving, and Reuben, 1974). In the present paper we compare the changes which we have observed in the maximum amplitude of the accelerocardiogram during handgrip in normal subjects and in patients with heart disease.

Subjects and methods

The six normal subjects (group 1), who performed handgrip without cardiac catheterization, were all volunteer members of staff aged between 26 and 35 years. The patients comprised 12 with dominant aortic stenosis (group 2), 3 of whom had mild aortic regurgitation and 2 of whom had coexistent coronary artery disease; and 16

with myocardial disease (group 3) caused by coronary atherosclerosis in 13 and idiopathic congestive cardiomyopathy in 3. The mean age (\pm SD) of the patients in group 2 was 55.9 ± 9.9 years, and in group 3, 48.4 ± 8.6 years. All patients were in sinus rhythm at the time of the study and none had clinical or haemodynamic evidence of mitral valve disease. Resting haemodynamic data are

summarized in Tables 1 to 3. Of the 12 patients in group 2, 10 had electrocardiographic evidence of left ventricular hypertrophy. Left ventriculography was performed with the patients of group 3 in the right anterior oblique position and showed a dyskinetic area in 4 (Table 1). Coronary arteriography was performed by the Judkins technique (Judkins, 1968). Of the patients in group 3, 8

TABLE 1 *Resting catheterization data*

Group 2 (aortic stenosis)				Group 3 (myocardial disease)		
Case	Aortic valve gradient (mmHg)	Calculated aortic valve area (cm ²)	Cardiac index (l/min per m ²)	Case	Coronary angiography	Contraction on left ventriculography
GB	35	0.43	1.72	JA	3-vessel disease	Poor
LB	34	1.13	2.72	DC	3-vessel disease	Good
AC	38	0.65	1.87	JC	3-vessel disease	Good
RC	79	0.72	4.18	WF	Normal	Good
JD	10	—	3.80	TG	3-vessel disease	Poor
PD	76	0.60	2.90	JK	3-vessel disease	Good
TL	77	1.10	3.10	JL	3-vessel disease	Good
AM	60	0.53	2.40	FM	Normal	Good
HS	43	0.90	3.30	JM	1-vessel disease (LAD)	Anterior aneurysm
AT	85	0.40	2.16	CM	3-vessel disease	Poor
TW	87	0.52	2.40	DM	2-vessel disease (LAD, RCA)	Apical aneurysm
AW	49	0.95	3.49	CP	3-vessel disease	Anterior hypokinesis
Group Mean	56	0.72	2.92	JR	Normal	Poor
SEM	7	0.08	0.22	JS	1-vessel disease (LAD)	Good
				GT	3-vessel disease	Good
				GW	2-vessel disease (LAD, RCA)	Inferior hypokinesis

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

TABLE 2 *Effects of handgrip in group 2*

Case	Heart rate (beats/min)		LV syst. press. (mmHg)		Ao syst. press. (mmHg)		Ao diast. press. (mmHg)		LVEDP (mmHg)		LV max. dp/dt (mmHg/s)		DE (μ V)	
	Control	Grip	Control	Grip	Control	Grip	Control	Grip	Control	Grip	Control	Grip	Control	Grip
GB	76	82	163	182	132	147	86	92	20	23	1870	2540	1100	1005
LB	60	79	210	240	200	225	95	120	24	45	1890	3040	380	450
AC	50	68	210	265	180	210	80	95	14	19	1780	2400	705	710
RC	94	98	203	215	116	121	75	85	18	20	1600	1800	342	480
JD	65	73	120	160	110	150	70	87	11.5	19	1330	1550	785	1000
PD	109	110	210	215	110	130	80	97	21	32	1560	1900	860	1020
TL	62	76	230	320	167	245	72	98	—	—	2150	3180	763	763
AM	72	81	220	258	105	134	65	75	11.5	18.5	500	620	470	551
HS	94	101	150	172	82	93	61	72	—	—	2500	2620	1195	885
AT	63	68	233	250	127	154	78	84	21	26	1450	1650	450	350
TW	81	83	240	250	140	155	90	100	15	15	1820	1960	689	826
AW	70	78	219	240	180	204	100	111	24	24	1580	1950	245	280
Group Mean	75	83	201	231	138	164	79	93	18	24	1670	2100	650	705
SEM	5	4	11	13	10	13	4	4	2	3	140	205	—	—

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

TABLE 3 *Effects of handgrip in group 3*

Case	Heart rate (beats/min)		LV syst. press. (mmHg)		LVEDP (mmHg)		LV max. dp/dt (mmHg/s)		DE (μ V)	
	Control	Grip	Control	Grip	Control	Grip	Control	Grip	Control	Grip
JA	47	58	135	175	20	21	2000	2000	670	695
DC	63	69	120	155	15	20	1070	1130	823	795
JC	60	62	190	215	15	20	1780	1930	613	527
WF	81	88	160	180	18.5	25	960	1060	790	630
TG	65	90	125	168	15	29.5	1820	2180	600	670
JK	53	57	125	140	16	20	1120	1250	372	453
JL	76	82	125	148	18	21	2360	2800	660	670
FM	61	71	120	157	11	18.5	2150	3170	685	820
JM	76	80	120	130	22	28	870	1000	475	434
CM	110	113	—	—	31	40	1100	1150	477	425
DM	81	85	117	137	13.5	15.5	1390	1530	490	565
CP	59	76	115	143	18	22	850	820	680	670
JR	60	72	100	145	12	21	845	1040	397	426
JS	67	68	130	135	20	25	1850	1790	632	794
GT	70	78	112	140	12	14	1190	1300	562	585
GW	76	87	120	140	12	13	1840	2780	370	430
Group										
Mean	68	77	128	154	17	22	1450	1700	575	595
SEM	4	4	6	6	1	2	130	180	—	—

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

had sustained a previous myocardial infarction and I was in cardiac failure, which was controlled by medical treatment, at the time of the study.

An electrocardiogram, recorded from praecordial leads, was displayed simultaneously with the accelerocardiogram on an ultraviolet recorder (Honeywell Recording Oscillograph, Type 1185 Mark 2). The accelerocardiogram transducer was attached to the chest wall overlying the fifth rib, internal to the apex beat, by means of an adhesive disc. All recordings were made during normal respiration, with the subjects supine.

The accelerometer is a cylindrical metal transducer, 2 cm in diameter, incorporating a strain gauge (Pixie Transducer, Endevco Laboratories Ltd., U.K.) on a cantilever spring, the free end of which is a 420 mg lead bob. When an acceleration is applied to the base of the transducer, the movement of the lead bob relative to the base depends upon the mass of the bob, the stiffness of the spring, and the acceleration applied. The output of the instrument has been shown to be linear up to 0.5 *g*, using analysis of pendular motion (Reuben and Littler, 1973), which is well in excess of any acceleration recorded during this study. Further details of the instrument have already been published (Bew *et al.*, 1971; Reuben and Littler, 1973).

Heart rate was calculated from the average of 10 consecutive RR intervals measured at a paper speed of 100 mm per second, while the maximum amplitude of the accelerocardiogram (DE in Fig. 1) was averaged over 20 consecutive beats, each measured to the nearest millimetre, at a paper speed of 25 mm per second. For convenience the accelerocardiogram data are expressed in microvolts (μ V) using a 0.5 millivolt square wave as a

standard. We made no attempt to calibrate the tracings in units of acceleration because variations in chest wall thickness, transducer coupling, and position of the heart render comparison of absolute values between subjects meaningless (Reuben and Littler, 1973). Furthermore, such a calibration is tedious to perform (Reuben and Littler, 1973).

The patients were studied during diagnostic cardiac catheterization after the collection of resting haemodynamic data but before angiography. On the day before catheterization each subject was familiarized with the handgrip procedure. Beta adrenergic blocking drugs were discontinued over the 72 hours preceding catheterization, but all other medication was administered as

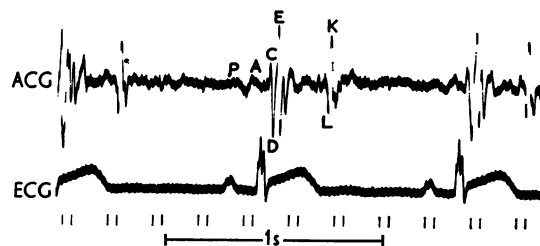


FIG. 1 *The pattern of the praecordial accelerocardiogram.*

Below: electrocardiogram.

Above: praecordial accelerocardiogram.

DE = maximum amplitude of the praecordial accelerocardiogram.

TABLE 4 Group mean changes during handgrip

	Heart rate (beats/min)				LV syst. pressure (mmHg)				Ao diast. pressure (mmHg)			
	Control	Handgrip	% change	P	Control	Handgrip	% change	P	Control	Handgrip	% change	P
Group 1												
Mean	68 (3)	78 (3)	+13 (3)	<0.005	114 (5)	138 (8)	+21 (3)	<0.001	78 (6)	91 (5)	+18 (4)	<0.02
(SEM)												
Group 2												
Mean	75 (5)	83 (4)	+11 (2)	<0.001	201 (11)	231 (13)	+15 (4)	<0.001	79 (4)	93 (4)	+18 (3)	<0.001
(SEM)												
Group 3												
Mean	68 (4)	77 (4)	+11 (2)	<0.001	128 (6)	154 (6)	+21 (3)	<0.001	—	—	—	—
(SEM)												

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

usual up to the time of the studies. One hour before catheterization the patients were sedated with 5 mg diazepam (Valium-Roche) orally.

In the patients in group 2 left ventricular pressure was recorded by means of a Brockenbrough catheter, after transseptal catheterization of the left atrium, and central aortic pressure by means of a Formocath catheter introduced into the right femoral artery by the Seldinger technique. In the patients in group 3 only left ventricular pressure was measured, after the Formocath had been manipulated across the aortic valve. Peak left ventricular systolic pressure, post 'a' wave left ventricular end-diastolic pressure, aortic systolic and diastolic pressures (group 2 only), and left ventricular maximum dp/dt, were recorded on an ultraviolet recorder (Shandon Southern Instruments Ltd., U.K.) before, during the final 30 seconds of, and 4 minutes after handgrip. Left ventricular dp/dt was obtained by electronic differentiation of the pressure signal, using a device whose response was uniform to 50 Hz. Resting cardiac output was measured by the indicator dilution method, using indocyanine green as the indicator and a Waters X 300 cuvette densitometer. In the patients with aortic stenosis the mean simultaneous aortic valve gradient was measured at rest and the valve area was calculated from Gorlin's formula (Gorlin and Gorlin, 1951).

In the normal subjects arterial blood pressure was measured by sphygmomanometry before, during, and after handgrip, the cuff being applied to the non-exercising arm. In the normal subjects handgrip was performed using a standard strain gauge dynamometer, whereas the patients gripped a partially inflated sphygmomanometer cuff. Each subject's maximum grip strength was first determined and each was then instructed to maintain 30 per cent maximum voluntary contraction for 3 minutes, a level of isometric exercise which has previously been shown to consistently elicit increases in heart rate and blood pressure (Fisher *et al.*, 1973; Kivowitz *et al.*, 1971; Payne, Horwitz, and Mullins, 1973). Care was taken to ensure that the subjects did not perform a Valsalva manoeuvre, as empha-

sized in previous studies (Fisher *et al.*, 1973; Helfant *et al.*, 1971; Kravenbuehl *et al.*, 1973).

The changes which occurred during handgrip are expressed as the mean change for the group \pm one standard error of the mean. Statistical analysis was performed by Student's t-test.

Results

The results are summarized in Tables 2 to 6 and Fig. 2.

A. Heart rate

In the normal subjects (group 1) handgrip increased group mean heart rate from 68 to 78 beats a minute, an increase of 13 ± 3 per cent ($P < 0.005$).

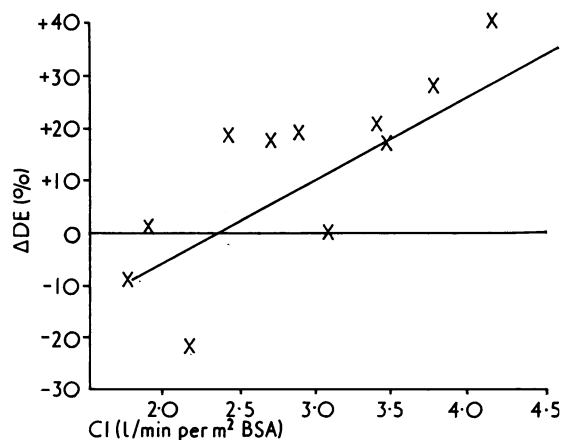


FIG. 2 Correlation between the percentage change in the maximum amplitude of the praecordial accelerocardiogram during handgrip (ΔDE) and resting cardiac index in patients with aortic stenosis. Regression equation: $\Delta DE = 14.9 CI - 35$ $r = 0.79$, $P < 0.01$.

LV max dp/dt (mmHg/s)				LVEDP (mmHg)				DE (μV)			
Control	Handgrip	% change	P	Control	Handgrip	% change	P	Control	Handgrip	% change	P
—	—	—	—	—	—	—	—	680	610	-10 (4)	<0.05
1670 (140)	2100 (205)	+25 (5)	<0.001	18 (2)	24 (3)	+35 (9)	<0.01	650	705	+8.5 (6)	>0.5 NS
1450 (130)	1700 (180)	+16 (5)	<0.005	17 (1)	22 (2)	+33 (6)	<0.001	575	595	+4 (4)	>0.3 NS

In the patients in group 2 mean heart rate increased from 75 to 83 beats a minute, a change of 11 ± 2 per cent ($P < 0.001$) and in group 3 mean heart rate increased from 68 to 77 beats a minute, a change of 11 ± 2 per cent ($P < 0.001$) (Tables 2 to 4). There were no significant differences in magnitude of induced tachycardia between the groups.

B. Blood pressure

In the normal subjects group mean systolic blood pressure increased from 114 to 138 mmHg (15.2 to 18.4 kPa), a change of 21 ± 3 per cent ($P < 0.001$). In group 2 the average left ventricular systolic pressure increased from 201 to 231 mmHg (26.7 to 30.7 kPa), a change of 15 ± 4 per cent ($P < 0.001$), and in group 3 left ventricular systolic pressure increased from 128 to 154 mmHg (17.0 to 20.5 kPa), a mean increase of 21 ± 3 per cent ($P < 0.001$). In group 1 diastolic blood pressure increased from a group mean value of 78 to 91 mmHg (10.3 to 12.1 kPa), a change of 18 ± 4 per cent ($P < 0.02$), and in group 2 aortic diastolic pressure increased from 79 to 93 mmHg (10.5 to 12.4 kPa), a change of 18 ± 3 per cent ($P < 0.001$) (Tables 2 to 4). Again, there were no significant differences in pressor response to handgrip between the groups.

C. Maximum dp/dt

Left ventricular maximum dp/dt increased by 25 ± 5 per cent, from a group mean value of 1670 to 2100 mmHg (222 to 279 kPa) per second in group 2 ($P < 0.001$), and by 16 ± 5 per cent, from 1450 to 1700 mmHg (193 to 226 kPa) per second ($P < 0.005$) in group 3 (Tables 2 to 4). There was no significant difference between groups 2 and 3 with respect to the rise in left ventricular maximum dp/dt ($P > 0.5$).

D. Left ventricular end-diastolic pressure

Group mean end-diastolic pressure increased from 18 to 24 mmHg (2.4 to 3.2 kPa) in group 2, a change of 36 ± 9 per cent ($P < 0.01$), and from 17 to 22 mmHg (2.3 to 2.9 kPa) in group 3, an increase of 33 ± 6 per cent ($P < 0.001$) (Tables 2 to 4). Again there was no significant difference ($P > 0.8$) between the groups.

E. Praecordial acceleration

In group 1, the maximum amplitude of the praecordial accelerocardiogram (DE) decreased significantly by an average value of 10 ± 4 per cent ($P < 0.05$) while in groups 2 and 3 DE increased insignificantly by 8.5 ± 6 per cent ($P > 0.5$) and 4 ± 4 per cent ($P > 0.3$), respectively (Tables 2 to 4). The response in the normal subjects differed significantly from that in the patients with aortic stenosis ($P < 0.02$) and from that in those with myocardial disease ($P < 0.01$), but there was no significant difference between the response of group 2 and that of group 3 ($P > 0.6$).

Individually, 50 per cent of the patients in each of groups 2 and 3 showed an abnormal response, i.e. a significant increase in DE. Our data were, therefore, closely examined to see if any haemodynamic differences existed between the patients with a normal response and those with an abnormal response. In neither group 2 nor group 3 did the two subgroups differ significantly with respect to the percentage changes in heart rate, left ventricular systolic pressure, aortic diastolic pressure, or left ventricular end-diastolic pressure (Tables 5 and 6). Though, in the patients with myocardial disease, the subgroup of patients with a significant increase in praecordial acceleration had a mean increase in left ventricular maximum dp/dt of 24 per cent compared with an increase of 7.5 per cent

TABLE 5 Haemodynamic data in subgroups of patients with aortic stenosis (group 2)

Case	Δ Heart rate (%)	Δ LV syst. press. (%)	Δ Ao diast. press. (%)	Δ LV max. dp/dt (%)	Δ LVEDP (%)	Resting LV max dp/dt (mmHg/s)	Resting LVEDP (mmHg)	Resting cardiac index (l/min per m ²)	Resting aortic valve gradient (mmHg)	Ao. valve area (cm ²)
Group 2A (abnormal response)										
LB	+23.5	+14.0	+26.0	+55.5	+87.0	1890	24	2.72	34	1.13
RC	+4.5	+6.0	+13.0	+12.5	+11.0	1600	18	4.18	79	0.72
JD	+12.0	+33.0	+24.0	+16.5	+65.0	1330	11.5	3.80	10	—
AM	+12.0	+17.0	+15.0	+24.0	+61.0	500	11.5	2.40	60	0.53
TW	+2.5	+4.0	+11.0	+8.0	0	1820	15	3.40	87	0.52
AW	+11.5	+9.5	+11.0	+23.5	0	1580	24	3.49	49	0.95
Mean	+11.0	+14.0	+18.5	+23.0	+37.0	1450	17	3.27	53	0.77
SEM	3.0	4.0	3.0	7.0	15.5	205	2.5	0.26	12	0.11
Group 2B (normal response)										
GB	+7.5	+12.0	+7.0	+36.0	+15.0	1870	20	1.72	35	0.43
AC	+27.0	+26.0	+19.0	+35.0	+36.0	1780	14	1.87	38	0.65
PD	+1.0	+2.0	+21.0	+22.0	+52.0	1560	21	2.90	76	0.60
TL	+19.0	+39.0	+36.0	+48.0	—	2150	—	3.10	77	1.10
HS	+7.0	+15.0	+18.0	+5.0	—	2500	—	3.30	43	0.90
AT	+8.0	+7.0	+8.0	+14.0	+24.0	1450	21	2.16	85	0.40
Mean	+11.5	+17.0	+18.0	+27.0	+32.0	1885	19	2.59	53	0.68
SEM	4.0	6.0	4.0	6.5	8.0	160	2.0	0.25	11.0	0.11
Group 2A versus group 2B										
P	>0.9	>0.6	>0.8	>0.7	>0.7	>0.1	>0.6	<0.05	>0.9	>0.5
	NS	NS	NS	NS	NS	NS	NS		NS	NS

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

in the remainder, this difference was not significant ($P > 0.3$). There were also no significant differences between the subgroups with respect to resting dp/dt, aortic valve gradient, or aortic valve area. However, the patients with aortic stenosis who responded to handgrip with an increase in praecordial acceleration had a significantly higher resting cardiac index, 3.27 as against 2.59 l/min per m² ($P < 0.05$) (Table 5). Furthermore, there was a significant linear correlation between the percentage change in praecordial acceleration and resting cardiac index (Fig. 2). Those patients with myocardial disease who responded abnormally in terms of DE had a significantly lower resting left ventricular end-diastolic pressure, 14 (1.9 kPa) as against 20 mmHg (2.7 kPa) ($P < 0.02$) (Table 6). Patients with a history of a previous myocardial infarction and those with dyskinetic areas did not differ from the remainder in their accelerocardiographic response to handgrip.

Discussion

The increases in heart rate, blood pressure, left ventricular end-diastolic pressure, and maximum dp/dt which we observed are comparable to those described in previous work (Fisher *et al.*, 1973; Grossman *et al.*, 1973; Helfant *et al.*, 1971; Kivo-

witz *et al.*, 1971; Kravenbuehl *et al.*, 1972, 1973; Payne *et al.*, 1973). Furthermore, the effects of handgrip in each of our three groups were of a similar order of magnitude (Table 4). Therefore, the differences in the response of the praecordial accelerocardiogram between the groups cannot be attributed to differences in the level of isometric exercise achieved, even though in the normal subjects handgrip was performed using a strain gauge dynamometer (Hume *et al.*, 1974) while the patients gripped a sphygmomanometer cuff. Our normal subjects were significantly younger than the patients in groups 2 and 3 but, in the various groups, there was no relation between age and the change in DE during handgrip. The subjects in group 1 were not studied during cardiac catheterization but, in 10 patients of groups 2 and 3 studied on the day before the procedure, the change in DE was similar to that which occurred during catheterization.

The interesting and unexpected finding which emerges from this study is that 50 per cent of patients in each of groups 2 and 3 responded abnormally to the stress of isometric exercise with an increase in DE. This subgroup of patients could not be distinguished from the remainder in terms of

TABLE 6 *Haemodynamic data in subgroups of patients with myocardial disease*

Case	Δ Heart rate (%)	Δ LV syst. press. (%)	Δ LV max. dp/dt (%)	Δ LVEDP (%)	Resting LV max. dp/dt (mmHg/s)	Resting LVEDP (mmHg)
<i>Group 3A (abnormal response)</i>						
TG	+28.5	+34.5	+20.0	+97.0	1820	15
JK	+6.5	+11.5	+12.0	+25.0	1120	16
FM	+14.0	+31.0	+47.5	+68.0	2150	11
DM	+4.0	+17.0	+10.0	+15.0	1390	13.5
JR	+16.5	+45.0	+47.0	+75.0	845	12
JS	+2.0	+4.0	-3.0	+25.0	1850	20
GT	+10.5	+25.0	+9.0	+17.0	1190	12
GW	+12.5	+16.5	+51.0	+8.0	1840	12
Mean	+12.0	+23.0	+24.0	+41.0	1525	14
SEM	3.0	5.0	7.5	12.0	160	1
<i>Group 3B (normal response)</i>						
JA	+18.0	+30.0	0	+5.0	2000	20
JC	+2.0	+13.0	+8.5	+33.0	1780	15
DC	+9.5	+29.0	+5.5	+33.0	1070	15
WF	+8.5	+11.0	+10.5	+35.0	960	18.5
JL	+7.0	+18.5	+18.5	+17.0	2360	18
CM	+3.0	—	+4.5	+29.0	1100	31
JM	+5.0	+8.5	+15.0	+27.0	870	22
CP	+22.5	+24.0	-3.5	+22.0	850	18
Mean	+9.5	+19.0	+7.5	+25.0	1375	20
SEM	2.5	3.5	2.5	3.5	205	2
<i>Group 3A versus group 3B</i>						
P	>0.5 NS	>0.5 NS	>0.3 NS	>0.2 NS	>0.5 NS	<0.02

Conversion factor from Traditional to SI Units: 1 mmHg \approx 0.133 kPa.

the adequacy of the test (Tables 5 and 6). The only interventions which have been shown to increase DE are dynamic exercise (Hume *et al.*, 1974) and increases in myocardial contractility induced by positively inotropic drugs (Reuben and Littler, 1973), particularly sympathomimetic amines. Though previous workers have shown an improvement in various indices of myocardial function during handgrip and have concluded that the normal response includes an increase in contractility (Grossman *et al.*, 1973; Helfant *et al.*, 1971; Kivowitz *et al.*, 1971; Kravenbuehl *et al.*, 1972; 1973), there is some evidence to suggest that this improvement in left ventricular performance is exclusively caused by the chronotropic effects of handgrip (Kravenbuehl and Rutishauser, 1973). The maximum amplitude of the praecordial accelerocardiogram is insensitive to changes in heart rate induced by atrial pacing (Reuben and Littler, 1973) and it also does not increase during handgrip in normal subjects (Hume *et al.*, 1974). Our observation that a significant proportion of cardiac patients shows an increase in DE during handgrip suggests that these patients increase left ventricular contractility during handgrip independently of any

effects of tachycardia. It seems to us that the most likely explanation is that these patients activate the beta adrenergic nervous system in response to the stress of isometric exercise.

In normal subjects beta adrenergic blockade does not greatly modify the cardiovascular response to isometric exercise and it has been concluded that the response in these subjects is relatively independent of this division of the autonomic nervous system (Macdonald *et al.*, 1966; Shaver *et al.*, 1972). Plasma catecholamine levels have been shown to increase excessively during dynamic exercise in patients with cardiac failure (Braunwald, 1965; Braunwald and Chidsey, 1965; Chidsey, Harrison, and Braunwald, 1962; Harrison and Chidsey, 1962) and angina pectoris (Gazes, Richardson and Woods, 1959; Richardson, 1963). It seems plausible, therefore, that certain patients with impaired myocardial reserve might respond to the stress of isometric exercise with a compensatory increase in beta adrenergic drive. There is also evidence of increased beta adrenergic tone at rest in patients with cardiac failure (Braunwald and Chidsey, 1965; Chidsey *et al.*, 1965; Gaffney and Braunwald, 1963) and in patients with aortic

stenosis (Hamer and Fleming, 1969). Robinson and his colleagues have presented evidence that, in physiological situations in which sympathetic tone is increased at rest, the adrenergic nervous system plays a greater role in the mediation of certain circulatory reflexes (Robinson *et al.*, 1966). This may be applicable to the circulatory response to handgrip in those patients in whom sympathetic tone is appreciable at rest.

Our observation that the patients with aortic stenosis who failed to show an increase in praecordial acceleration were those with a low cardiac index (Table 5, Fig. 2) is interesting. A reduction in cardiac index in aortic stenosis is a late event in the natural history of the disease (Dexter *et al.*, 1958) and is said to signify the presence of left ventricular failure (Goldberg, Bakst, and Bailey, 1954; Gorlin *et al.*, 1955). It is possible that, when myocardial impairment reaches a critical level, the compensatory increase in sympathetic stimulation during handgrip becomes insufficient to increase left ventricular contractility and the response, in terms of the praecordial accelerocardiogram, reverts to 'normal'. Previous work has shown a reduction in the responsiveness of the heart to electrical stimulation of the sympathetic nerves in advanced, experimental cardiac failure (Covell, Chidsey, and Braunwald, 1966). The pathological counterpart of this phenomenon might be the reduction in myocardial norepinephrine stores which has been described in severe cardiac failure (Braunwald, 1965; Braunwald and Chidsey, 1965; Chidsey *et al.*, 1963, 1965).

The patients with myocardial disease who failed to increase praecordial acceleration during handgrip had a significantly higher resting left ventricular end-diastolic pressure than those who did (Table 6). While this would conform to our previous suggestion that patients with poor myocardial function are unable to increase praecordial acceleration during handgrip despite increased beta adrenergic activation, the mechanism underlying a raised left ventricular end-diastolic pressure in coronary artery disease is not altogether clear and may equally well be an impairment of left ventricular diastolic compliance rather than pump failure (Bristow, Van Zee, and Judkins, 1970). However, in the patients with aortic stenosis, in whom altered compliance is even more likely, there was no difference in left ventricular end-diastolic pressure between the two subgroups of patients. Nevertheless, we do not feel justified in concluding that patients with coronary heart disease and a raised left ventricular end-diastolic pressure necessarily have impaired systolic function of the left ventricle. An association between increased left ventricular

filling pressure and the presence of segmental abnormalities of contraction in coronary artery disease has been demonstrated (Herman and Gorlin, 1969) and, more recently, handgrip has been shown to induce or accentuate localized wall motion abnormalities (Ludbrook, Karliner, and O'Rourke, 1974). This could be the explanation for our observation that the patients with higher left ventricular end-diastolic pressures failed to increase praecordial acceleration during handgrip (Table 6).

Although the discussion of our results is largely speculative, the hypotheses advanced in this section may readily be tested and should serve to stimulate further studies into the mechanisms by which cardiac patients adapt to stress.

References

- Bew, F. E., Pickering, D., Sleight, P., and Stott, F. D. (1971). 'Pixie' cardiography. Accelerometer applications to phonocardiography and displacement cardiography in childhood. *British Heart Journal*, **33**, 702.
- Braunwald, E. (1965). The control of ventricular function in man. *British Heart Journal*, **27**, 1.
- Braunwald, E., and Chidsey, C. A. (1965). The adrenergic nervous system in the control of the normal and failing heart. *Proceedings of the Royal Society of Medicine*, **58**, 1063.
- Bristow, J. D., Van Zee, B. E., and Judkins, M. P. (1970). Systolic and diastolic abnormalities of the left ventricle in coronary artery disease. *Circulation*, **42**, 219.
- Chidsey, C. A., Braunwald, E., and Morrow, A. G. (1965). Catecholamine excretion and cardiac stores of norepinephrine in congestive heart failure. *American Journal of Medicine*, **39**, 442.
- Chidsey, C. A., Braunwald, E., Morrow, A. G., and Mason, D. T. (1963). Myocardial norepinephrine concentration in man. Effects of reserpine and of congestive heart failure. *New England Journal of Medicine*, **269**, 653.
- Chidsey, C. A., Harrison, D. C., and Braunwald, E. (1962). Augmentation of the plasma norepinephrine response to exercise in patients with congestive heart failure. *New England Journal of Medicine*, **267**, 650.
- Chung, D. C. W., Chamberlain, J. H., and Seed, R. G. F. L. (1974). The effect of haemodynamic changes on maximum blood flow acceleration at the aortic root in the anaesthetized open-chest dog. *Cardiovascular Research*, **8**, 362.
- Covell, J. W., Chidsey, C. A., and Braunwald, E. (1966). Reduction of the cardiac response to post-ganglionic sympathetic nerve stimulation in experimental heart failure. *Circulation Research*, **19**, 51.
- Dexter, L., Harken, D. E., Cobb, L. A., Novack, P., Schlant, R. C., Phinney, A. O., and Haynes, F. W. (1958). Aortic stenosis. *Archives of Internal Medicine*, **101**, 254.
- Fisher, M. L., Nutter, D. O., Jacobs, W., and Schlant, R. C. (1973). Haemodynamic responses to isometric exercise (handgrip) in patients with heart disease. *British Heart Journal*, **35**, 422.
- Gaffney, T. E., and Braunwald, E. (1963). Importance of the adrenergic nervous system in the support of circulatory function in patients with congestive heart failure. *American Journal of Medicine*, **34**, 320.
- Gazes, P. C., Richardson, J. A., and Woods, E. F. (1959). Plasma catecholamine concentrations in myocardial infarction and angina pectoris. *Circulation*, **19**, 657.

- Goldberg, H., Bakst, A. A., and Bailey, C. P. (1954). The dynamics of aortic valvular disease. *American Heart Journal*, **47**, 527.
- Gorlin, R., and Gorlin, S. G. (1951). Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves, and central circulatory shunts. *American Heart Journal*, **41**, 1.
- Gorlin, R., McMillan, I. K. R., Medd, W. E., Matthews, M. B., and Daley, R. (1955). Dynamics of the circulation in aortic valvular disease. *American Journal of Medicine*, **18**, 855.
- Grossman, W., McLaurin, L. P., Saltz, S. B., Paraskos, J. A., Dalen, J. E., and Dexter, L. (1973). Changes in the inotropic state of the left ventricle during isometric exercise. *British Heart Journal*, **35**, 697.
- Hamer, J., and Fleming, J. (1967). Effect of propranolol on left ventricular work in aortic stenosis. *British Heart Journal*, **29**, 871.
- Harrison, D. C., and Chidsey, C. A. (1962). Assessment of sympathetic nervous system activity during exercise in congestive heart failure (abstract). *Circulation*, **26**, 729.
- Helfant, R. H., DeVilla, M. A., and Meister, S. G. (1971). Effect of sustained isometric handgrip exercise on left ventricular performance. *Circulation*, **44**, 982.
- Herman, M. V., and Gorlin, R. (1969). Implications of left ventricular asynergy. *American Journal of Cardiology*, **23**, 538.
- Hume, L., Irving, J. B., and Reuben, S. R. (1974). The effects of beta blockade on the praecordial accelerocardiogram. *Scottish Medical Journal*, **19**, 200.
- Judkins, M. P. (1968). Percutaneous transfemoral selective coronary arteriography. *Radiologic Clinics of North America*, **6**, 467.
- Kivowitz, C., Parmley, W. W., Donoso, R., Marcus, H., Ganz, W., and Swan, H. J. C. (1971). Effects of isometric exercise on cardiac performance. The grip test. *Circulation*, **44**, 994.
- Krayenbuehl, H. P., and Rutishauser, W. (1973). Hemodynamic consequences and clinical significance of the handgrip test. *European Journal of Cardiology*, **1**, 5.
- Krayenbuehl, H. P., Rutishauser, W., Schoenbeck, M., and Amende, I. (1972). Evaluation of left ventricular function from isovolumic pressure measurements during isometric exercise. *American Journal of Cardiology*, **29**, 323.
- Krayenbuehl, H. P., Rutishauser, W., Wirz, P., Amende, I., and Mehmehl, H. (1973). High fidelity left ventricular pressure measurements for the assessment of cardiac contractility in man. *American Journal of Cardiology*, **31**, 415.
- Ludbrook, P., Karliner, J. S., and O'Rourke, R. A. (1974). Effects of submaximal isometric handgrip on left ventricular size and wall motion. *American Journal of Cardiology*, **33**, 30.
- Macdonald, H. R., Sapru, R. P., Taylor, S. H., and Donald, K. W. (1966). Effect of intravenous propranolol on the systemic circulatory response to sustained handgrip. *American Journal of Cardiology*, **18**, 333.
- Noble, M. I. M., Stubbs, J., Trenchard, D., Else, W., Eisele, J. H., and Guz, A. (1972). Left ventricular performance in the conscious dog with chronically denervated heart. *Cardiovascular Research*, **6**, 457.
- Noble, M. I. M., Trenchard, D., and Guz, A. (1966a). Left ventricular ejection in conscious dogs. I. Measurement and significance of the maximum acceleration of blood from the left ventricle. *Circulation Research*, **19**, 139.
- Noble, M. I. M., Trenchard, D., and Guz, A. (1966b). Effect of changing heart rate on cardiovascular function in the conscious dog. *Circulation Research*, **19**, 206.
- Payne, R. M., Horwitz, L. D., and Mullins, C. B. (1973). Comparison of isometric exercise and angiotensin infusion as stress test for evaluation of left ventricular function. *American Journal of Cardiology*, **31**, 428.
- Reuben, S. R., and Littler, W. A. (1973). Praecordial accelerometry: an indirect assessment of left ventricular performance. *European Journal of Clinical Investigation*, **3**, 324.
- Richardson, J. A. (1963). Circulating levels of catecholamines in acute myocardial infarction and angina pectoris. *Progress in Cardiovascular Diseases*, **6**, 56.
- Robinson, B. F., Epstein, S. E., Beiser, G. D., and Braunwald, E. (1966). Control of heart rate by the autonomic nervous system. Studies in man on the inter-relation between baroreceptor mechanisms and exercise. *Circulation Research*, **19**, 400.
- Shaver, J. A., Martin, C. E., Reddy, P. S., Thompson, M. E., and Leon, D. F. (1972). Effects of selective autonomic blockade on cardiovascular responses to isometric exercise (abstract). *Circulation*, **46**, Suppl. II, 219.
- Winter, P. J., Deuchar, D. C., Noble, M. I. M., Trenchard, D., and Guz, A. (1967). Relationship between the ballistocardiogram and the movement of blood from the left ventricle in the dog. *Cardiovascular Research*, **1**, 194.

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